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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/331,808	01/27/2000	BJORN H. LINDQVIST	100084.410	2109

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EXAMINER
WESSENDORF, TERESA D

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 11/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/331,808	Applicant(s) LINDQVIST ET AL.	
	Examiner T. D. Wessendorf	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *19 July 2002 and 29 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *19-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *19-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/9/01 has been entered.

Status of Claims

Claims 1-18 have been cancelled and claims 19-37 have been added in the amendment of 10/9/01. However, claims 19-20 which had been added in the Amendment of 1/11/01 are still active and have not been cancelled.

The numbering of claims 19-37 in the Amendment of 10/9/01 is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 19-37 have been renumbered 21-39.

Claims 19-39 are active in the application.

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 30 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

The specification does not provide a specific utility for the in vitro peptide expression library. The specification, page 29, second complete paragraph, recites generically that the instant library has utility in screening protocols for identifying compounds with appropriate biochemical, biological or structural properties, for example to identify peptides or proteins which have certain biochemical activity in a defined assay. With this method peptides or proteins may be identified with inhibitory or stimulating properties which **may** have utility

for example, in the pharmaceutical field. However, an intended use is not equivalent to a specific use required by the statute. The library, per se, does not have a specific utility, except as employed in the screening process to screen for a compound that may have a pharmaceutical utility. Thus, only after further research would it seem that a specific and substantial credible utility might be found for a compound isolated from said library (and not for the library, itself). This further characterization, however, is part of the act of invention and until it has been undertaken, applicant's claimed invention is incomplete, as it lacks a specific utility for the library.

The court in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claimed library is of no or of yet undetermined structure, function or biological significance. There is no

evidence, either in the prior art or instant specification, or any line of reasoning that would support a conclusion that the library of the instant application was, as of the filing date, useful for anything. Until some actual and specific significance can be attributed to the library or even the compounds, isolated and identified from the library, an artisan would be required to perform additional experimentation in order to determine the use of the claimed library. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696. Further, In *Brenner*, the Court approved a rejection for failure to disclose any utility for a compound where the compound was undergoing screening for possible compounds the utility of which has also not been identified. *Brenner*, 148 USPQ at 690. Here, there is not even a single evidence of a compound isolated from the library, let alone the compounds present in the instant library. *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use

for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.') The instant claim is drawn to an in vitro expression library and compounds that can be isolated from said library, neither of which has no determine function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the library of the instant application was, as of the filing date, useful, except to form a collection to isolate a compound which utility has also not been specifically set forth.

Claim 30 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear,

> concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 21-24, 26-28, 30-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the cis-protein P2A, does not reasonably provide enablement for any cis-proteins or functional fragments, variants or derivative thereof; any amplifiable gene or DNA library or degenerate and functionally equivalent sequences thereof; target molecule; reporter moiety and bifunctional molecular probe. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of the enabling disclosure is not commensurate in scope with the broad claimed invention. The specific embodiments provided in the specification are drawn to a method by which a library cis-proteins of P2A is amplified by specific library of

primers. There is no other cis-proteins, let alone, a fragment, variant or derivatives of said proteins that have been amplified by any kind of library primers to create a library of cis-proteins binding DNA. Furthermore, the claims recite broadly for any DNA that encodes a binding moiety, a display moiety for any type of DNA cis acting proteins. To determine a single variable of the numerously infinite numbers of undefined parameters encompassed by the claims require undue amount of experimentation.

The factors to be considered in the determination of undue experimentation are disclosed in In re Wands (USPQ 2d 1400:CAFC 1988), which include:

1. The Breath of the claims: The claims cover too numerous undefined or broad variables not only for each of the claimed different methods but also for the broad components employed in each method. Each of the claimed methods recites only two broad method steps and uses broad components in each of the methods such as the amplifiable gene library, DNA molecules encoding a binding moiety and a display moiety encoding for a cis-protein, fragments, variants, derivatives thereof of the cis-proteins, a DNA vector that contains a DNA sequence.

2. The nature of the invention: is such that DNA and peptides are so unpredictable in their mode of actions. For

example, because of the degeneracy of DNA molecules wherein a codon can encode two or more different residues, one can not predict a priori the outcome obtained for one DNA encoding compound to a multiple compounds embraced by the claimed methods and compounds. Furthermore, the polynucleotide amplification process whereby amplification products comprise a frequency of mutation, typically in the form of nucleotide misincorporation; potential aggregation and misfolding of the compounds occur in some prokaryotic expression systems.

3. The state of the prior art: as evident from the different prior art discussed in the Background is such that only specific screening of a specific library results in the desired compound. Screening is known to be a formidable task for a created library, especially for any kind of library with an undefined constituent.

4. The level of one of ordinary skill: is undoubtedly high, but the DNA and protein areas the skilled is working in, is known to be so highly or notoriously unpredictable that a skilled artisan has not predicted the outcome of a single DNA encoding cis proteins to other known proteins or especially to a yet unidentified cis-proteins.

5. The level of predictability in the art: is so high that one to date a skilled artisan has not extrapolated a single

finding for one compound to another compound, especially for the unrelated ones. Because of the degeneracy of the DNA molecule, it would not be predictable if the desired amino acids were the one obtained therein.

6. The amount of direction provided by the inventor and the presence or absence of working examples: is limited to the specific cis-proteins, P2A. There is nothing in the specification that extrapolates the findings to other cis-proteins or other cis-proteins included in the breath of the claims.

7. The quantity of experimentation necessary to make or use the invention based on the disclosure: is undue because of the reasons set forth above, and is nothing more than an invitation to experiment.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point

out and distinctly claim the subject matter which applicant regards as the invention.

1. Claims 21, 33, 34,36 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the step by which a population of peptides is specifically associated with DNA. It is not clear how the two steps of amplifying and expressing a library of peptides result with a specifically associated DNA or how the library is obtained. Furthermore, the term "amplifiable" is indefinite whether in fact any given gene library has been amplified simply by defining a DNA sequence encoding a binding moiety and a display moiety i.e., the components that amplify a given library is unclear, in the context of the claimed invention.

2. Claim 23 is unclear as to how the encoding sequence "is derived" from a cis-acting protein. The metes and bounds of the claimed functionally-equivalent fragment" is unclear i.e., in the context as to which function is considered equivalent to the cis-proteins; the variants, as it is not clear whether variations are done at the N or C or mid-part of the cis-

proteins, singly or in combinations; the kinds and length of derivatives obtained therein.

3. Claim 24 is indefinite, in the context of the claim, as to the step encompassed by the in vitro step.

4. It is not clear, within the claimed context, the term "corresponding", as recited in claim 26.

5. Claim 31 is indefinite in the recitation of different kinds of DNA molecule. Also, it is not clear as to the DNA sequences that are considered degenerate and/or functionally equivalent since the metes and bounds of said sequences are not positively set forth in the claims or specification. The use of colon(:) in protein:DNA binding is unclear. If this is a covalent binding then a positive recitation of said bonding is better.

6. Claim 33 is unclear as to the "desired" properties. The basis by which a property is the desired one is not clearly set forth in the specification or claims.

7. Claim 36 is indefinite as it is not clear as to the step or difference between the step of direct or indirect assessing of the target bound probe.

8. Claim 37 is indefinite as to what constitute a "bifunctional" molecular probe, in the context of the claims.

9. Claim 38 is indefinite as to the kind and/or numbers of properties exhibited by each member in a library. This claim has been treated as it depends on claim 28 since it erroneously depends on cancelled claim 11.

10. Claims 19, 20 and 38 depend on cancelled claim 11 (for claims 19 and 38) and claim 1 (for claim 20).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al (Virology, 1996) either alone, or in view of Mattheakis et al (US 5,922,545).

Liu et al discloses at page 158 under the Materials and Methods section up to page 150, col. 1 a method of producing cis-proteins comprising of constructing a plasmid containing a mutated cis-proteins and fragments of the P2A genes which had been amplified by DNA primers as shown in Fig 1. Each of the created plasmid is then transformed into a specific strain

(BL21) for the production of the proteins. Overexpression of gene A leads to formation of inclusion bodies. The A protein was purified to homogeneity by one-step affinity chromatography (corresponds to the claimed method of purifying recited in claim 38). Liu further discloses, page 160, col. 2 that the A proteins remains covalently joined of the 5'end after cleavage. Liu discloses at page 163, Discussion section, that the expressed protein can rejoin its DNA encoding sequence (i.e., a specifically associated DNA encoding cis-protein, as claimed) where joining is by covalent bond to the nick 5' DNA. Liu does not expressly disclose that the plasmids produced are a library of DNA-binding cis-proteins. However, Mattheakis discloses, col. 6, line 59 up to col. 7, an improved method of producing a library in vitro wherein the DNA encoding a protein is linked to the DNA i.e., a coupled in vitro transcription/translation system to generate the mRNA encoding proteins from a library of mRNA. Mattheakis further discloses at col.5, lines 46-50 that the polypeptide is associated with a cDNA copy of the temple MRNA. Mattheakis also, discloses, at col. 17, lines 52, an in vitro process for a DNA-binding protein that can bind to DNA in a sequence-specific manner (e.g., bind to specific predetermined nucleotide sequences). The nascent polypeptide library members comprise an encoding polynucleotide (or DNA primer bound

thereto), which comprises a sequence bound by the sequence specific DNA binding protein. Mattheakis defines polynucleotide binding protein as encompassing DNA-binding proteins, whether sequence-specific or sequence insensitive. Mattheakis discloses at col. 7, line 48 up to col. 9, line 62, a method of screening for a library to find a library member that has substantial binding affinity to a receptor. Accordingly, it would have been obvious to one having an ordinary skill in the art at the time the invention was made to prepare a library of the DNA encoding cis-proteins of Liu. The Lui reference, itself, implicitly teaches constructing a library. In constructing the plasmids numerous clones were obtained, which implicitly would be a library of cis-proteins. Even if Liu does not explicitly recites a library, Mattheakis discloses said library and provides the motivation for making a library i.e., in creating and screening a library, a diverse populations of the desired compound can be produced from which one can obtained a library member that has substantial or improved properties e.g., greater or optimum binding affinity to a receptor that would lead to a compound with a pharmacological effect.

In view of the new grounds of rejection and new found prior art, the argument in the REMARKS of 10/0/01 is moot.

Claims 23, 29, 38 and 39 are obvious over the disclosure of Liu at page 159, col. 1; page 163, col. 1 and page 160, col. 1.

Claims 30, 31, 33, 34 are obvious over the teachings of Mattheakis, specifically the Examples at col. 42, line 59 up to col. 52,line 15.

Claim 36 and 37 are obvious over the disclosure of Mattheakis at col. 21, lines 56-63; col. 82, claim 4.

No claim is allowed.

REASSIGNMENT OF LOCATION

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit **1639**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
November 4, 2002